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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/578,171	05/04/2006	Ulrike W. Klueh	MTI/101/PC/US	4607

2543 7590 02/19/2009

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EXAMINER	
SAJJADI, FEREYDOUN GHOTB	
ART UNIT	PAPER NUMBER
1633	
MAIL DATE	DELIVERY MODE
02/19/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/578,171	KLUEH ET AL.	
	Examiner	Art Unit	
	FEREYDOUN G. SAJJADI	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 January 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,9,14-16,19,20,25,27,28,37-39,51,52,54,59 and 66-75* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,9,14-16,19,20,25,27,28,37-39,51,52,54,59 and 66-75* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *5/4/2006* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/29/2006; 8/29/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This action is in response to papers filed January 2, 2009. Applicant's response to the second restriction requirement of December 1, 2008 has been entered. Claim 75 has been amended. No claims were cancelled, or newly added. Currently, claims 1-4, 9, 14-16, 19, 20, 25, 27, 28, 37-39, 51, 52, 54, 59 and 66-75 are pending in the application.

Election/Restrictions

Applicants previously elected of Group I, drawn to an artificial tissue system or an artificial implant system comprising said artificial tissue system, with traverse.

Applicants' election of the species of biological cells, biological matrices, gel and inflammation, is acknowledged. In view of the teachings of the cited prior art, the restriction between the species of biological cells and engineered cells is hereby withdrawn.

Applicants' election of (Basement membrane and cytokines bound to the basement membrane) and normal vascular stem cells and engineered stem cells, and the elected basement membrane - normal vascular stem cell combination as recited in claim 75 is *non sequitur*. The election for the combination of the matrix material and cellular component does not appear to be a single specific combination, and further, it is unclear whether the species recited in parenthesis is an equivalent to the cell, matrix combination. In the interest of compact prosecution the election has been treated as the "basement membrane and normal or engineered vascular stem cell combination". The elections were made without traverse.

As the restriction is still deemed proper, the requirement for restriction is maintained and hereby made FINAL. Please note that after a final requirement for restriction, the Applicants, in addition to making any response due on the remainder of the action, may petition the Commissioner to review the requirement. Petition may be deferred until after final action on or allowance of claims to the invention elected, but must be filed not later than appeal. A petition will not be considered if reconsideration of the requirement was not requested. (See § 1.181.).

Applicants timely responded to the restriction (election) requirement in the reply filed August 28, 2008.

Claims 1-4, 9, 14-16, 19, 20, 25, 27, 28, 37-39, 51, 52, 54, 59 and 66-75 are under current examination. The claims have been examined commensurate with the elected invention, and the species of the invention.

Information Disclosure Statement

The information disclosure statements (IDS) submitted on August 26, 2008 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statements have been considered by the examiner, and indicated as such on Applicants' IDS form.

The IDS submitted on August 26, 2006 contains a reference to U.S. Patent No.: 6,479,729. However, this patent is not by Moussy et al. and thus has not been considered by the Examiner.

Objections to the Specification

The brief description of the figures is objected to, because Figure 22 (p. 8), sets forth the nucleic acid sequence of mouse VEGF without the recitation of a SEQ ID NO.

Failure to Comply with Nucleotide and /or Amino Acid Sequence Disclosures 37CFR §1.821-1.825

37 CFR 1.821 (a) states: Nucleotide and/or amino acid sequences as used in §§1.821 through 1.825 are interpreted to mean an unbranched sequence of four or more amino acids or an unbranched sequence of ten or more nucleotides. 37 CFR 1.821 (d) states: Where the description or claims of a patent application discuss a sequence that is set forth in the "Sequence Listing " in accordance with paragraph (c) of this section, reference must be made to the sequence by use of the sequence identifier, preceded by "SEQ ID NO:" in the text of the description or claims, even if the sequence is also embedded in the text of the description or claims of the patent application.

Neither of the sequence depicted in Figure 22, nor the brief description of the drawings refer to the sequence by SEQ ID NO. Applicants are required to provide both a paper and CRF sequence listing in concordance with the sequence depicted in Figure 22. The instant application

may be placed in compliance with 37 CFR 1.821-1.825 by amending the Figure or the brief description of the Figure to refer to appropriate SEQ ID NO.

Claim Rejection - 35 USC § 112- New Matter

The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 66 is rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art (hereafter the Artisan), that the inventor(s), at the time the application was filed, had possession of the claimed invention. 37 CFR §1.118 (a) states that "No amendment shall introduce new matter into the disclosure of an application after the filing date of the application".

Dependent claim 66, newly introduced by the amendment dated August 29, 2008 is directed to the implant system of claim 28, further comprising a subsystem configured to test the effectiveness of the artificial tissue system in extending the life of the implant. Applicants state that the claim reflects the limitation of cancelled claim 36. However, neither the instant specification nor original claim 36 contain such limitations. Original claim 36 was directed to a system for testing the effectiveness of an implant comprising the artificial tissue system, and simply read on a sensor. The limitation of claim 36 was further not described in the specification. A subsystem configured to test the effectiveness of the artificial tissue system in extending the life of the implant does not constitute the subject matter of claim 36.

Thus, at the time the application was filed, an Artisan of skill would not recognize from the disclosure that Applicant was in possession of the subsystem for testing the effectiveness of the artificial tissue system in extending the life to the implant, as instantly claimed.

MPEP 2163.06 notes: "If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. *In re Rasmussen*, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)." MPEP 2163.02 teaches that

"Whenever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed...If a claim is amended to include subject matter, limitations, or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application. MPEP 2163.06 further notes "When an amendment is filed in reply to an objection or rejection based on 35 U.S.C. 112, first paragraph, a study of the entire application is often necessary to determine whether or not "new matter" is involved. Applicant should therefore specifically point out the support for any amendments made to the disclosure". This is a new matter rejection.

Claim Rejections - 35 USC § 112- Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 9 and 75 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 9 is unclear. The claim is directed to an artificial tissue system comprising an implantable device wherein the biological system comprises a mammal. However, while a mammal may comprise an artificial tissue system and an implantable device, it is not clear how a said artificial tissue system and implantable device may have a mammal inserted therein.

Claim 75 is unclear. The claim is directed to a Markush grouping that recites a basement membrane and normal vascular stem cells; (basement membrane and cytokines bound to basement membrane) and normal vascular stem cells; etc. It is unclear whether the limitations recited in parentheses are separate or distinct from the preceding grouping, whether they further define the preceding combination, and if separate, why they are partly parenthesized. It is yet further unclear whether the basement membrane is equivalent to the matrix material.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-4, 9, 14-16, 19, 20, 25, 27, 28, 37, 39, 51, 52, 54, 67, 68, 69, 70, 72 and 73 are rejected under 35 U.S.C. 102(e) as being anticipated by Sayler et al. (U.S. Patent No.: 6,673,596; filed Dec 2, 1999).

The claims encompass an artificial tissue system, comprising a matrix configured for biological contact with an implantable device and a plurality of cells supported by said matrix.

Sayler et al. teach an *in vivo* biosensor device comprising a genetically engineered bioreporter for detecting glucose, glucagons or insulin target analytes in the body of an animal; the bioreporter device encapsulated on an integrated circuit. Further teaching controlled drug delivery systems capable of being directly or indirectly controlled by the detection device that provide drugs such as insulin to the animal in response to the amount of target analyte present in the body fluids (Title an Abstract; limitation of claims 14, 15 and 68).

Sayler et al. further teach that the monitoring and regulating the level of analytes may be carried out in the tissues and circulatory system of a human (first column, lines 22-24; limitation of claims 9 and 39). The bioreporter preferably comprises a plurality of eukaryotic cells that produce a reporter polypeptide in response to the presence of the target analyte. Exemplary mammalian cells are human cells such as islet β -cell, or immortal stem cells, comprising one or more nucleic acid segments that encode the reporter polypeptide (column 3, lines 54-66; limitation of claims 2, 4, 70, 72 and 73).

Sayler et al. additionally teach that the biosensor may consist of bioengineered living cells entrapped or encapsulated in a polymeric matrix, or in suspension behind a semi-permeable membrane. Examples of matrices include sol-gel or microporous hydrogels (column 23, lines 34-

53). Biochips may be coated with Matrigel, a basement membrane material that promotes attachment of epithelial cells. An alternate approach suspends the cells in Matrigel and allows it to form a gel on the surface of the biochip. The cells are then immobilized in the basement membrane material (column 35, lines 42-47; limitation of claims 1, 16, 20, 25, 27, 28, 37, 51, 52, 54, 69 and 75).

Sayler et al. state that post-transplantation host-rejection effects can be minimized through immunoisolation techniques by enclosing non-host cells in hydrogel membranes; and that host ejection of the implanted biosensor is not a an issue if cells from the host are used for the biosensor construction (column 25, lines 14-17 and 26-27; limitation of claims 3, 19 and 67).

Therefore by teaching all the limitations of the claims, Sayler et al. anticipate the instant invention as claimed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 28, 37, 38, 59, 66, 70, 71 and 74 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sayler et al. (U.S. Patent No.: 6,673,596; filed Dec 2, 1999), in view of Soykan et al. (U.S. Patent Application Publication 2001/0000802; effective filing date: Dec. 20, 2000).

The claims embrace an artificial implant system, comprising an implantable device, a matrix configured for biological contact with said implantable device and a plurality of cells supported by said matrix, wherein the cells induce cellular growth and neovascularization, wherein the implant system further comprises a system for testing the effectiveness of said implant.

Sayler et al. describe an *in vivo* biosensor device comprising a genetically engineered bioreporter for detecting glucose, glucagons or insulin target analytes in the body of an animal; the bioreporter device encapsulated on an integrated circuit. Further teaching controlled drug delivery systems capable of being directly or indirectly controlled by the detection device that provide drugs such as insulin to the animal in response to the amount of target analyte present in the body fluids (Title an Abstract).

Sayler et al. state the bioreporter preferably comprises a plurality of eukaryotic cells that produce a reporter polypeptide in response to the presence of the target analyte. Exemplary mammalian cells are human cells such as islet β-cell, or immortal stem cells, comprising one or more nucleic acid segments that encode the reporter polypeptide (column 3, lines 54-66). Sayler et al. additionally state that the biosensor may consist of bioengineered living cells entrapped or encapsulated in a polymeric matrix, or in suspension behind a semi-permeable membrane.

While Sayler et al. do not specifically describe the cells as inducing cellular growth and neovascularization, and the implant system further comprising a subsystem, such was known in the prior art.

Soykan et al. describe an implantable system that includes a carrier and eukaryotic cells, which produce and release a therapeutic agent and a stimulating element for stimulating the release of the therapeutic agent. The system can also include a sensing element for monitoring a physiological condition and triggering the stimulating element to stimulate the delivery device to release the therapeutic agent (Abstract). Soykan et al. state that the drug-eluting cells can be genetically engineered autologous endothelial cells that line the walls of blood vessels, that secrete vasodilatory, thrombolytic or angiogenic factors, such as vascular endothelial growth factor (VEGF), (paragraphs [0031] and [0034], p. 4; paragraph [0042], p. 5; limitation of claims 38, 71 and 74).

Soykan et al. further describe their implant as further comprising a second polymer composition coating at least a portion of the first polymer composition and cells containing a coagulation inhibitory or anti-inflammatory compound (paragraph [0062], pp. 7-8, bridging; limitation of claim 59).

With respect to the implant further comprising a subsystem configured to test the effectiveness of the artificial tissue system Soykan et al. state that the systems of the present invention include a second implantable device that includes a stimulation element, preferably in contact with a sensing element, and monitors the patient and detects when a stimulus needs to be sent to the cells to trigger release of one or more therapeutic agents (paragraph [0069]; p. 8). As the implant comprises a sensor, the second implantable device constitutes a subsystem sensor that monitors the effectiveness of the implant.

It should be noted that endothelial cells are a component of vascular structures and VEGF is well known for its inherent ability to promote neovascularization, and must necessarily do so in the biological system.

As stated in MPEP 2112, the express, implicit, and inherent disclosures of a prior art reference may be relied upon in the rejection of claims under 35 U.S.C. 102 or 103. "The inherent teaching of a prior art reference, a question of fact, arises both in the context of anticipation and obviousness." *In re Napier*, 55 F.3d 610, 613, 34 USPQ2d 1782, 1784 (Fed. Cir. 1995). Moreover, there is no requirement that a person of ordinary skill in the art would have recognized the inherent disclosure at the time of invention, but only that the subject matter is in fact inherent in the prior art reference.

"When the structure recited in the reference is substantially identical to that of the claims, claimed properties or functions are presumed to be inherent." See MPEP 2112.01 or *In re Best*, 195 USPQ 430, 433 (CCPA 1997). As stated in MPEP 2112: The express, implicit, and inherent disclosures of a prior art reference may be relied upon in the rejection of claims under 35 U.S.C. 102 or 103. "The inherent teaching of a prior art reference, a question of fact, arises both in the context of anticipation and obviousness." *In re Napier*, 55 F.3d 610, 613, 34 USPQ2d 1782, 1784 (Fed. Cir.1995) (affirmed a 35 U.S.C. 103 rejection based in part on inherent disclosure in one of the references). See also *In re Grasselli*, 713 F.2d 731, 739, 218 USPQ 769, 775 (Fed. Cir. 1983).

The teachings of Sayler et al. and Soykan et al. are directed to implants and tissue systems comprising genetically altered cells. Therefore, it would have been *prima facie* obvious for a person of ordinary skill in the art, to combine their respective teachings and to genetically alter the implanted cells to secrete VEGF to induce cellular growth and neovascularization, as instantly claimed, with a reasonable expectation of success, at the time of the instant invention. A person of ordinary skill in the art would have been motivated to utilize endothelial cells transformed with a VEGF gene in the implant system of Sayler et al., because such was expressly taught by Soykan et al. to deliver a therapeutic product to a patient.

Conclusion

Claims 1-4, 9, 14-16, 19, 20, 25, 27, 28, 37-39, 51, 52, 54, 59 and 66-75 are not allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to FEREYDOUN G. SAJJADI whose telephone number is (571)272-3311. The examiner can normally be reached on 6:30 AM-3:30 PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Fereydoun G Sajjadi/

Examiner, Art Unit 1633